

**Amendments to the Claims:**

The following list of claims will replace all prior versions of the claims in the application:

1. (*Canceled*)

2. (*Currently amended*) A method for assessing toxicity of a compound of interest, comprising:

a) exposing tissue samples comprising a set of genes to the compound of interest;

b) measuring the hybridization signal of each gene in the set of genes to the compound of interest;

c) creating gene expression profiles using ~~two or more~~ a plurality of variables, wherein the ~~two or more plurality of~~ variables ~~include~~ includes time and dose;

identifying patterns within the gene expression profiles that demonstrate time stability and dose dependence, wherein a pattern is defined where a change in gene expression progresses in a same direction with time and increased dose, and selecting gene expression profiles that fit the patterns;

d) creating one or more composite variables from the selected gene expression profiles of (c);

e) creating one predictive composite from the composite variables of (d), wherein the one predictive composite comprises a binary value indicating one of a positive or negative ; and

~~— f g ) comparing the results of (e f) to a profile of a known compound to determine whether there is a toxicological response to the compound of interest.~~

3. (*Previously presented*) The method of Claim 2, wherein the set of genes comprises 10-100,000 genes.

4. (*Currently amended*) The method of Claim 2, wherein the ~~two or more~~ plurality of variables further ~~include~~ includes treatment-6.

5. (*Canceled*)

6. (*Currently amended*) The method of Claim 2, wherein the step (b) of measuring further comprises averaging the hybridization signals of a portion of the genes having a lowest signal intensity to determine a background level; and

selecting for further analysis the hybridization signals having a difference signal intensity that exceed a pre-selected percentage of exceeds the background level, wherein the difference signal intensity is taken relative to a mismatch control for each gene.

7. (*Currently amended*) The method of Claim 2, wherein the step (e) of identifying comprises performing contrast analysis.

8. (*Currently amended*) The method of Claim 2, wherein the step (e) of identifying comprises performing cluster analysis.

9. (*Currently amended*) The method of Claim 2, wherein the step (d) of creating one or more composite variables comprises performing principal components analysis.

10. (*Currently amended*) The method of Claim 2, wherein the one predictive composite variables of (e) is created using logistic regression or discriminant analysis.

11.-22. (*Canceled*)

23. (*Currently amended*) The method of Claim 2, wherein the step (d) of creating one or more composite variables comprises performing partial least squares analysis.

24. (*Currently amended*) The method of Claim 2, wherein the step (d) of creating one or more composite variables comprises performing factor analysis.

25. (*Previously presented*) The method of Claim 2, wherein the compound of interest is acetaminophen.

26. (*Currently Amended*) A method for assessing the toxicity of a compound of interest, comprising:

a) exposing tissues comprising a set of genes to the compound of interest;

b) generating gene expression data corresponding to ~~the~~ a hybridization signal of each gene in the set of genes ~~to the compound of interest;~~

e) identifying patterns in the gene expression data that demonstrate time stability and dose dependence, wherein a pattern is defined where a change in gene expression

progresses in a same direction with time and increased dose, and selecting a subset of the gene expression data which are time stable and dose dependent that fit the patterns;

~~d)~~ combining the subset of gene expression data into defining one or more composite variables to assign each gene to a pattern using the subset of the gene expression data; and

e) converting the one or more composite variables into one predictive composite measure for determining a probability of similarity;

wherein the probability of similarity comprises an indicator of toxicological effect of the compound of interest.

27. (*Currently amended*) The method of claim 26, wherein the step (e) of identifying comprises performing contrast analysis.

28. (*Currently amended*) The method of claim 26, where the step (d) of defining one or more composite variables comprises performing principal components analysis.

29. (*Currently amended*) The method of claim 28, wherein the step (e) of converting comprises performing a logistic regression using the principal components identified in ~~step (d)~~ the principal components analysis.

30. (*Currently amended*) The method of claim 26, wherein the ~~tissue samples~~ tissues are liver, kidney, brain, spleen, pancreas and lung.

31. (*Currently amended*) The method of claim 26, wherein the step (b) of generating gene expression data further comprises averaging the hybridization signals of a portion of the genes having a lowest signal intensity to determine a background level; and

selecting for further analysis the hybridization signals having a difference signal intensity that exceed a pre-selected percentage of exceeds the background level, wherein the difference signal intensity is taken relative to a mismatch control gene for each gene.

32. (*Previously presented*) The method of Claim 2, wherein the tissue samples are liver, kidney, brain, spleen, pancreas and lung.

33. (*Previously presented*) The method of Claim 2, wherein the compound of interest is CCl<sub>4</sub>.

34. (*New*) A method for assessing the toxicity of a compound of interest, comprising:
- exposing tissues comprising a set of genes to the compound of interest;
  - generating gene expression data corresponding to a hybridization intensity of each gene in the set of genes;
  - performing analysis of variants to identify patterns in the gene expression data that demonstrate time stability and dose dependence, wherein a pattern is defined where a change in gene expression progresses in a same direction with time and increased dose;
  - selecting a subset of gene expression data that fits the patterns;
  - applying factor analysis to the subset of gene expression data to define one or more composite variables; and
  - applying logistic regression to convert the one or more composite variables into one predictive composite measure of toxicological effect of the compound of interest.
35. (*New*) The method of claim 34, where the step of performing an analysis of variants comprises analyzing time stability and dose dependence simultaneously.
36. (*New*) The method of claim 34, wherein the step of performing an analysis of variants comprises cluster analysis or contrast analysis.
37. (*New*) The method of claim 34, wherein the step of applying factor analysis comprises performing principal components analysis or least squares analysis.